## REMARKS

After careful consideration of the Examiner's Office Action, Applicants have cancelled Claims 1-15 and have elected to pursue the subject matter of newly added Claims 16-30. New claims 16-30 are drawn to methods of using quercetin and derivatives thereof to ameliorate symptoms associated with osteoporosis. In particular, independent Claim 16 is drawn to administering to a subject a therapeutic agent which comprises quercetin or at least one derivative thereof but lacks calcium. Support for this claim is found in each of the Examples as well as throughout the specification. Independent Claim 21 is drawn to administering to a subject a therapeutic agent which consists essentially of quercetin or at least one derivative thereof. Support for this claim can found in each of the Examples and throughout the specification. Independent Claim 26 is drawn to administering to a subject a therapeutic agent which comprises quercetin or at least one derivative thereof thereby increasing the trabecullar bone area of the subject. Support for this claim is found in Example 3 (see, for example, Table 6 on page 22 and lines 1-15 on page 23) and elsewhere in the specification. Support for each of the dependent claims is found in originally filed claims 2-5 and throughout the specification. Accordingly, no new matter has been added by this amendment.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects Claims 1-15 under 35 U.S.C. § 112, second paragraph as allegedly failing to particularly point out and distinctly claim subject matter of the invention. In particular, the Examiner asserts that the claims are "unclear as to how many derivatives must be in the claimed therapeutic agent." Additionally, the Examiner asserts that Claims 2-4 contain phrases that do not clearly state "which derivatives are intended to be within the scope of the claim."

Applicants have cancelled claims 1-15 and added new claims 16-30. These new claims are not drawn to therapeutic agents comprising quercetin derivatives, but rather, these claims are drawn to methods of using therapeutic agents, which comprise quercetin or at least one quercetin derivative, to ameliorate symptoms associated with osteoporosis. Additionally, the newly added dependent claims use proper Markush language to recite the quercetin derivatives that are used in the claimed methods. Accordingly, Applicants respectfully submit that new Claims 16-30 are definite as required by 35 U.S.C. § 112, second paragraph.

Claim Rejections Under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(b)

Claims 1-5, 11, 14 and 15 stand rejected as being anticipated under either 35 U.S.C. § 102(a) or 35 U.S.C. § 102(b). Each of Claims 1-5, 11, 14 and 15 are drawn to therapeutic agents containing quercetin derivatives for the treatment of osteoporosis. The Examiner asserts that one or more of these claims are anticipated by any one of six cited references. Applicants respectfully disagree, however, to expedite prosecution of this patent application, Applicants have cancelled Claims 1-5, 11, 14 and 15 and have added new Claims 16-30, which are drawn to methods of administering a therapeutic agent comprising quercetin or at least one derivative thereof to ameliorate symptoms associated with osteoporosis. In the remarks that follow, Applicants address in turn each of the Examiner's rejections in view of newly added claims 16-30.

The Examiner rejects Claims 1-5 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,774,229 (Jordan) or alternatively by Sullivan *et al.* In particular, the Examiner asserts that both Jordan and Sullivan *et al.* disclose the administration of quercetin derivatives.

Each of the newly added claims are drawn to methods of administering a therapeutic agent comprising quercetin or at least one derivative thereof to ameliorate symptoms associated with osteoporosis. Neither Jordan nor Sullivan *et al.* disclose the use of these quercetin derivatives to treat osteoporosis. Accordingly, Applicants respectfully submit that neither Jordan nor Sullivan *et al.* anticipate the newly added claims.

The Examiner rejects Claims 1 and 11 under 35 U.S.C. § 102(b) as allegedly being anticipated by Derwent abstract 1995-151458 (Ito *et al.*). In particular, the Examiner asserts that Ito *et al.* disclose "a drink comprising quercetin glycoside, cyclodextrin and vitamin C.

Each of the newly added claims are drawn to methods of administering a therapeutic agent comprising quercetin or at least one derivative thereof to ameliorate symptoms associated with osteoporosis. The Derwent abstract 1995-151458 does not disclose the use of quercetin glycoside for the treatment of osteoporosis. Accordingly, Applicants respectfully submit that this reference does not anticipate the newly added claims.

The Examiner rejects Claims 1-3 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 6,063,383 (Hsu *et al.*). In particular, the Examiner asserts that Hsu, *et al.*

disclose "a pharmaceutical suppository composite comprising quercetin, isoquercetin, isorhamnetin and rutin."

Each of the newly added claims are drawn to methods of administering a therapeutic agent comprising quercetin or at least one derivative thereof to ameliorate symptoms associated with osteoporosis. Hsu *et al.* do not disclose the use of the suppository composite for the treatment of osteoporosis. Accordingly, Applicants respectfully submit that this reference does not anticipate the newly added claims.

The Examiner rejects Claims 1, 2, 14 and 15 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,478,579 (Sawruk). In particular, the Examiner asserts that Sawruk discloses administration of a tablet comprising isoquercitrin and calcium to treat osteoporosis.

A close reading or Sawruk reveals that this reference discloses the administration of isoquercitrin (or alternatively a few select quercetin derivatives) always together with calcium as a treatment for osteoporosis. Sawruk explains that flavonol aglycone glycosides chelate calcium and facilitate its delivery to bone (see column 3, lines 33 to 57). Sawruk makes no disclosure of the administration of quercetin or derivatives thereof in the absence of calcium. Furthermore, Sawruk discloses only modest improvement in bone density (approximately 5.4%) when isoquercitrin is co-administered with calcium in the amounts disclosed therein.

Claims 16-30 are drawn to a methods of administering a therapeutic agent comprising quercetin or at least one derivative thereof to ameliorate symptoms associated with osteoporosis. Many of these claims require that the therapeutic agent lack calcium. Other claims require that the administration of the therapeutic agent result in an increase in the amount of trabecullar bone area that is not achieved in Sawruk. Accordingly, Applicants respectfully submit that Sawruk does not anticipate the newly added claims.

The Examiner rejects Claims 1 and 2 under 35 U.S.C. § 102(a) as allegedly being anticipated by Horcajada-Molteni *et al.*. In particular, the Examiner asserts that Horcajada-Molteni *et al.* disclose "rat food formulated to contain rutin, and that administration of the food prevents bone loss in ovariectomized rats."

Applicants respectfully submit that none of the newly added claims recite the administration of rutin to ameliorate the symptoms associated with osteoporosis. As such, the newly added claims are not anticipated by Horcajada-Molteni *et al.*.

Claim Rejections Under 35 U.S.C. § 103(a)

The Examiner rejects Claims 1 and 6-14 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sawruk. In particular, the Examiner states that Sawruk suggests several possible formulations of quercetin derivatives and motivates a skilled artisan to prepare such formulations because Sawruk discloses "that any conventional carrier or physical form for administration could be employed."

Applicants have cancelled claims 1 and 6-14. The newly added claims are not drawn to pharmaceutical preparations of quercetin or derivatives thereof. Accordingly, Applicants respectfully submit that the newly added claims are not obvious over Sawruk.

The Examiner also rejects Claims 1 and 5 under 35 U.S.C. § 103(a) as allegedly being unpatentable over International Publication WO92/13851 (Romeo, *et al.*). In particular, the Examiner states that Romeo discloses 3,7,4'-trimethylquercetin and 3,7,3',4'-tetramethylquercetin. The Examiner also states that a skilled artisan would be motivated to prepare such compounds in combination with a pharmaceutically acceptable carrier because Romeo discloses "the use of these compounds in pharmaceutical preparations."

Applicants have cancelled claims 1 and 5. The newly added claims are not drawn to pharmaceutical preparations of quercetin or derivatives thereof. Accordingly, Applicants respectfully submit that the newly added claims are not obvious over Romeo.

## CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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